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Austin P. Haller
University of Nebraska Medical Center

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C A R C I N O M A O F T H E C E R V I X

Its

HISTORY SYMPTOMATOLOGY DIAGNOSIS

By

Austin P. Haller

S E N I O R T H E S I S

University of Nebraska

College of Medicine

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CARCINOMA OF THE CERVIX UTERI.

History -- Symptomatology -- Diagnosis.

Cancer of the uterus, being first described in a concise manner by Hippocrates, has been the great stumbling block to all Doctors and workers in medicines associated sciences since that time. Excepting the clinical and morphological description, relatively little progress was made in any line of the study of the disease until the 19th century and the general use of an improved microscope, and improved technique of tissue staining. During the last century, and especially the last fifty years an immense amount of study and research has been under progress. Much knowlege has been gained in all of the phases of the work especially the microscopic anatomy, life history and pathology of cancer, as well as the chemical and staining reactions of the cells. As yet no practical, accepted solution has been advanced for the immediate etiology or treatment of the disease.

Each phase of the study is a life's work in itself, and so,-- far be it from me, the author, to attempt to discuss in this thesis the whole huge field of Carcinoma. Carcinoma of the cervix uteri is in itself a life's work, and not to be this lightly regarded. If he may be permitted to select certain phases of the subject Carcinoma of the Cervix Uteri, and in so doing elect to discuss the historical background, the symptomatology and diagnosis, the author shall attempt to do so in a logi-

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cal and reasonable manner.

The historical references found lead to the belief that the disease which we now designate as cancer was known to the ancients at least two thousand years ago. Healy says that one may safely say that for three thousand five hundred years or thereabouts, the disease known as cancer has been recognized, studied and treated.

These ancient people worked without lens or microscope, and hence could discover or determine nothing concerning the minute structure of tumors and the various tissue manifestations with which they confused cancer. Undoubtedly many errors in diagnosis were made, and many diseases now accepted as of non-malignant nature were considered malignant by earlier observers. Leprosy, which is so familiar to every person who has read the Bible, probably covered many forms of ulcerating sores, as well as certain scaly skin diseases, and did not necessarily mean only the leprosy of which we speak today.

It is not to be wondered at, therefore, that imagination was given full play in the evolution of the elaborate theories of etiology which have marked the development of the cancer problem; nor is it surprising that the therapeutic history of the disease is one of the most fantastic of any in the annals of medicine and surgery.

References to cancer of the uterus in ancient history are remarkably scarce, as far as the author could determine, notwithstanding the allusions made by num-

erous writers that any attempt to trace the ancient history of cancer would take more space than could be given to the subject in their books, due, they say, to the enormous quantities of literature on the subject, ^{The literature on the subject} has been abstracted and presented in chronological order as fully as was possible from the material at my command.

Cancer is first mentioned in the Papyrus Ebers (B.C. 1500) and, although very slightly, in the oldest remnants of the literature of India and Persia. They treated it by excision and by a variety of escharotics, including the Egyptian arsenical ointment.

In the language of the ancient Hindu's, Kanda mean't utero-vaginal tumors. Saith they, these may arise from mechanical injury of the part. When air produces the disease, the tumor is dry and of a dirty or yellow color, and has furrows on its surface. When phlegm produces the tumore, it is like the color of the indigo flower, and is very itchy.

Herodotus mentions that Democedes (B.C. 520) cured Atossa, the daughter of Darius Hystaspis, of breast cancer.

Hippocrates (B.C. 460-375) received from earlier days a considerable body of descriptive facts regarding cancer of the skin, breast, uterus and internal organs. The humoral pathology then disseminated conceptions of the origin of cancer. Deficiency or excess of blood, mucous or bile, formed the basis of all disease.

Hippocrates, himself, about 460 B.C. is the first

to mention cancer of the uterus as such. He said that when we find that the uterus has become hard and projects into the genital parts, then we know there are indications of a tendency to cancerous degeneration. Clysters are to be recommended. While incurable, fumigations may be tried.

The Hippocratic writers were quite familiar with cancer of superficial organs. They introduced the terms carcinosis, apparently signifying a non-healing ulcer, even hemorrhoids, while carcinoma indicated a malignant tumor. A hard type of tumor was distinguished from open carcinosis or carcinoma. Our term scirrhus has almost the original significance. In their book Diseases of Women, scirrhus enduatum of the cervix is mentioned.

Celsus (B.C. 30--A.D. 38) distinguished several gross varieties of cancer, although he does not mention cancer of the cervix. He excised breast cancer, advising against removal of the pectoralis major muscle. Treatment by charcoal was employed by Cato, and a variety of crude internal remedies are mentioned by Pliny.

Galen (A.D. 131-203), the founder of experimental physiology and pathology, failed to make any significant advance in the conception of cancer, but the presentation of the humoral doctrine of atra bilis in his writings formed a scripture which dominated medical thought for more than a thousand years. Swellings were secundam naturam (gravid uterus), or praeter naturam (true tumors). The pneuma, composed of solid parts and four fluids,

blood, mucus, yellow and black bile, ruled the processes of the body. Cancer developed from the concentration of the black bile. Suppression of menses and hemorrhoids, preventing the discharge of black bile, were chiefly responsible for cancer, which appeared where the bile gravitated-- in face, lips, breast, etc.

No modern writer has been able to reflect the thought of that period or to explain the firm entrenchment of the crude humeral theories. Since capable logic could not have been lacking, one must suppose that religious and esthetic tendencies in the races unfitted the human mind for natural thought regarding the structure and functions of the human body. For internal cancer, of which little was known, a diet, chiefly vegetable was recommended. Walnuts were specifically forbidden.

Diagnosis rested chiefly on the cause of the disease, while treatment by excision, ligation of vessels and cautery was comparatively successful. Leonides of Alexandria (A.D. 180) broke away from Hippocrates' conservatism, dissected out breast cancer extensively, cutting through healthy tissue with knife and cautery and approached closely to the modern technique of this operation.

In the Byzantine period considerable progress was made in the description of various tumors. Paulus of Aegina separated chronic metritis from uterine cancer.

Aretaeus (A.D. 250) gives a description of sores of the cervix. He states that they are dangerous only in

those cases where the pain gets accelerated and the woman uneasy. From the sore there is discharged putrid matter, intolerable even to themselves; it is exasperated by touching and by medicines and irritated by almost any mode of treatment. The veins in the uterus are swelled up with distension of the surrounding parts. Febrile heat, general restlessness, and hardness are present, as in malignant disease; the ulcers being of a fatal nature, obtaining also the appellation of cancers. Another cancer, no ulceration anywhere, swelling hard and intractable, which distends the whole uterus; but there are pains, also, in the other parts where it drags to it. Both these carcinomatous sores are chronic and deadly, but the ulcerated is worse than the unulcerated, both in smell and pains, in life and in death.

Oribasius (A.D. 325-395) remarks that cancer of the cervix is incurable, but that we should alleviate the pain by means of opium pessaries.

Archigenes, in the time of Trajan, removed mammary and uterine cancers.

Aetius of Amida in Mesopotamia (A.D. 502-575) was physician to the Emperor Justinian. His work is largely compiled from the writings of Rufus of Ephesus, Leonides of Alexandria, Soranus and Archigenes. He gave a surprisingly clear picture of cancer of the uterus saying that some ulcerate, and some do not, as in cancer of the breast. When there is no ulceration, the tumor found around the os uteri is hard and resistant to the touch,

uneven, prominent, feculent in color, red or livid; sharp pains are felt in the groins, vulva, and loins, and these are increased by manual examination and by various medications.

He continues on with his description saying that should the cancer be an ulcerated one, in addition to pain, hardness and swelling, we find ulcers spreading and irregular, and for the most part foul, prominent, and white in color; some, however, appear feculent, livid red and bloody.

The discharge that comes from cancers is always thin, watery, black or reddish-yellow, with a strong odor. Occasionally we have hemorrhage, and other signs which indicate inflammation of the uterus. The complaint, as Hippocrates said, is incurable, but may be relieved by baths of fenugreek and mallow and by cataplasms of a similar kind.

Various receipts are given for local treatment, but no operative measures are described. He warns the reader against touching growths if they are malignant in character.

No historical mention could be found of any knowledge, in Europe, of cancer of the uterus during the next chronological period -- the Dark Ages. The works of the Greeks and Romans were unknown to the ordinary man and were probably forgotten by all except the monks in their secluded monasteries. They were patiently copying the ancient manuscripts and were the means whereby knowledge

of the ancient writers has been preserved for more modern generations.

Avicenna, a Mohammedan, in the 10th century A.D. writes lengthily and with much detail on elongation and induration of the cervix, of flexion, of prolapses and of uterine tumors. He points out that cancer of the cervix is extremely grave.

From 900 A.D. until 1266 A.D. when we hear of Theodoric, Bishop of Cervia, in Italy, the literature is entirely bare of references to uterine cancer. Theodoric comes nearest to us of all the old medieval surgeons. His treatment of many practical problems is interesting for modern time. For instance, in his discussion of cancer, he says that there are two forms of the affection. One of them is a melancholy tumor, a constitutional tendency as it were, and occurs especially in the breasts of women or latent in the womb. This is difficult of treatment and usually fatal, he says. The other class consists of a deep ulcer with undermined edges -- and so being palpably not cancer really does not here concern us.

In 1360 A.D. we find that Guy de Chauliac taught that cancer should be treated at an early stage and preferably with the knife.

The oriental scientists may not have advanced our knowledge of cancer, but they maintained it and fortified the old argument, that early and thorough excision is the only radical cure for malignant disease; while one of them, Avenzoar, in the 12th century, was the wri-

ter to show us that the breast is not, after all, the commonest seat of cancer, but that the stomach and the uterus share its malignant honors.

Pare recognized cancer as such. He says that cancer is a product of melancholia and women more than men are its victims. He also mentioned a case in which he recognized spread of cancer as evidenced by metastasis.

Henri Francois Le Dran, 1749, boldly attached the cancer problem with no uncertain hand. At once he rebukes the sceptics, for he proclaims that cancer is curable -- not late cancer, but cancer that is perceived early, and is cut out betimes. He perceived that cancer frequently occurs in the uterus, where it makes known its presence by dribbling hemorrhage and he says that he has known fresh cancer to arise in different parts even after extirpation of that which appeared at first. In this case, he notes, the bones may break by being affected by some cancerous tumor. He considered the above facts good evidence of an intrinsic abnormality of the lymph.

With the end of the eighteenth century there began a great outpouring of cancer writings, and names crowd the text, such as Hunter, Fearon, Pearson, and Adams at the end of the eighteenth century; Home, Abernethy and Bichat at the beginning of the nineteenth. None now dealt with cancer of the cervix as a separate subject but wrote on cancer in general. The medical profession now were beginning to interest themselves in the microscopic anatomy, the etiology and life cycle of the mali-

nant growths.

Fearon maintained that inflammation is the cause of the disease, and invariably and universally connected with it. He said that metastases partake of the same general characteristics as the primary tumor; that the spread of cancer is by contact dissemination, as well as through the lymphatics and blood-vessels; and that the rapidity of its development into a generalized constitutional ailment is dependant largely on the lymph supply of the parts.

Abernethy, also on the right track, said that the structure of a tumor is something like the part in which it grows.

Bichat advanced the study still further. He really laid the foundation of all future study of tumors when he said that every tissue has its own diseases.

John Rodman and William Farr, 1818 and 1822 respectively, seemed to take steps backward. John Rodman maintained that cancer is contagious. Farr was convinced that cancer is a constitutional disease somewhat of the nature of syphilis.

Broussais, a pupil of Bichat, taught that all tumors, including cancer, were but forms of chronic inflammation consequential on organic irritation. Williams, in comment, says that the extreme generalization, suddenly sprung on a scientific world hesitating between the old humoral doctrines and the nascent anatomico-pathological tentatives, captivated everyone, and the Broussaisian

system in an incredibly short time became supreme.

Soon, however, the microscope was finally and properly developed so that promptly the cellular structure of organized beings was discovered. We accord to Schleiden and to Schwann the demonstration of the famous cell theory, and the application by Schwann of this theory to the animal world, in 1838.

In this very year Johannes Muller published his work on tumor origin -- a work upon which are founded our modern conceptions of the cellular nature and pathogenesis of cancer, and of all other neoplasms. His descriptions satisfy the histological picture, but he falls short of meeting the modern conceptions of cancer's etiology. He ascribed the origin of cancer to aberration of the force inherent in a coagulable blood lymph which he called blastema.

Within little more than twenty years, 1859 to be exact, Virchow championed the cell theory as explained by Muller, but with this exception, that he eliminated the coagulable lymph or blastema origin of cells.-- Williams in paraphrasing his idea states that where a cell rises, there a cell must have previously existed, just as an animal can spring only from an animal, and a plant from a plant. Thus in place of the blastema, Virchow in his earlier day set up connective tissue as the substrate for cancer, and an abundance of supposed confirmation flowed to the master's hands from contemporary workers. But it still remained for Remak,

Thiersch, Waldeyer, and Billroth to reconstruct Virchow's tumor pathology with omission of his errors.

Robert Remak (1815-1865), a colleague at the Charite, from the onset a clear thinking and independent cellular pathologist, only overshadowed by Virchow, soon demonstrated by sound histological technique that skin cancers came from the epidermis and not from connective tissue. The surgeon, Carl Thiersch (1822-1895) of Erlangen, without a microtome, but with good razors and an ammoniated carmine and indigo stain, prepared colored serial sections of tumors from different organs with conclusive proof that epithelial tumors had an epithelial origin (1865). William Waldeyer (1836-1921), a pupil of the great histologist Henle, and one of the outstanding anatomists of modern times, confirmed this source of epithelial tumors in internal organs.

Cohnheim (1839-1884) will always be remembered as one of the great teachers of pathology in the nineteenth century. Aside from his studies on inflammation, embolism and infarction, Cohnheim is noted for his views on the origin of malignant growths. Impressed by the variety of congenital malformations that could be traced to accident or defect in the course of embryonic development, he conceived the idea that tumors might have a similar origin. He suggested that cells, with full capacity for orderly growth while in their normal relation to other cells, could become separated through an embryonic accident, and remain dormant in the iso-

lated state, until in later years some stimulus activated them, whereupon growth took place with all their old time vigor with the production of a tumor. This theory has had great influence upon the study of malignant growth, and, while largely abandoned today in its general applications, has proved highly fertile in the understanding of teratomas.

With the onset of antisepsis, in 1865, surgeons took courage to interfere in the early stages of an affection, an advantage particularly notable in the treatment of cancer. Radical excision has been advocated for centuries, but it is only within comparatively recent years, or since surgeons have come to understand the histopathology of cancer, that surgical technic has developed to such a degree of perfection as to enable one to say with assurance that it is possible to effect a cure of the disease by means of surgical intervention.

It has been said that more has been accomplished in the study of cancer during the past thirty years, or since the initiation of modern cancer research, than during the preceding fifteen hundred years. This renewed activity in the investigation of cancer, is believed by Bainbridge to be directly traceable to the success attendant upon the organized campaign against tuberculosis.

In America the inception of the movement for the study of cancer was largely due to the late Professor Roswell Park, who in 1899 was put in charge of a labor-

atory at Buffalo, New York, for cancer research. The primary object of this institution was a determination of the nature of the disease, and for medication and cure. The money for use was appropriated by the legislature of New York. It, therefore, was the first to establish a state institution devoted to the study of malignant disease.

The surgical department of the Harvard Medical School organized the Harvard Commission of the Harvard University in 1899. At first devoted to laboratory research only, in 1912 it began to make clinical researches in the disease.

In Germany a society called the Committee for Cancer Research was formed in 1900 and rapidly led to the formation of an International Association for Cancer Research. This latter body, swayed by political and personal issues, accomplished nothing and is of very little importance.

Other laboratories and Associations for cancer research may only be named for all are working along similar lines. There are the Cancer Research Laboratories, Middlesex hospital, and the Imperial Cancer Research Fund in England. The Royal Cancer Hospital in Glasgow, The Cancer Department of the Rockefeller Institute, the laboratory of the St. Louis Cancer Hospital, and the formation of the Crocker Cancer Fund in America. The Research Department of the New York Skin and Cancer Hospital and many many others.

There appears to be only one known way to successfully combat the high cancer mortality and that is by the recognition of the process in the earliest stages, or to better identify those lesions which are definitely known to be the forerunner of malignancy in a very large majority of cases.

The cervix because of its location is strikingly susceptible to infection, trauma and malignancy.

The Mortality Statistics record shows that in the registration area of the United States in nineteen twenty the number of deaths from cancer was one hundred and eleven thousand five hundred and sixty nine, corresponding to the crude rate of ninety five and nine tenths per one hundred thousand population, In striking contrast to the rate sixty-three in nineteen hundred is the high rate ninety-five and nine tenths in nineteen hundred twenty nine or a remarkable increase of fifty-two and two tenths percent. Cancer of the female genital organs causes fourteen and three tenths percent of all deaths from cancer. Thirty per cent of all cases of carcinoma occurring in women have origin in the uterus and about ninety-eight percent of these develop in the cervix. One woman out of every twenty-seven dies of uterine cancer.

Before the histological basis of cancer had been discovered, these growths were supposed by many to represent simply local manifestations of a constitutional dyscrasia, some claiming that the virus was present in

the blood, and that even if the affected organ was removed the cancer would nevertheless develop at some distant site. We now know that in the beginning cancer is essentially a local process, and that the apparently independent growths occurring later in other organs are really metastases from the primary tumor. This point has been proved not only by histological studies, but also by clinical experience, since if the primary growth can be removed by operation, before metastases have taken place, the patient is permanently cured.

The elements in cervical cancer that favor successful treatment are, according to Graves, as follows:

- (1) It is readily accessible in its early stages.
- (2) It usually, though not always, develops slowly.
- (3) It tends to distant metastasis comparatively late.
- (4) The initial symptoms are sufficiently distinctive to be recognized by patient and doctor.
- (5) In the early stages it may be cured by the knife, the cautery, or with radium.
- (6) On account of its anatomical location it is peculiarly fitted to radium treatment since in no other cancer of the body can the important principle of cross-firing be so favorably applied.

Laceration with its associated chronic irritating inflammation is not, to be sure, the only causative ele-

ment in cancer of the cervix uteri, but it is so in at least ninety per cent of all cases. This relationship between cervical cancer and traumatic irritation is altogether too constant and imitates far too completely the artificial production of cancer to be regarded as a post hoc coincidence.

Here then is a practical working-basis for a prophylaxis, which may theoretically be achieved, first by the avoidance of child-bed injuries to the cervix and secondly by timely repair of the cervical lesions which by virtue of their long-continued irritation may eventuate finally in malignant change.

Avoidance of child-bed injuries obviously depends on better obstetrics. That skillful obstetrics prevents cancer of the cervix seems well established by the comparative rarity of the disease among the well-to-do, and needs no special comment.

From a theoretic standpoint, and reasoning from the results of artificial cancer production, one may confidently say that it is not the initial rupture of the cervix wall that determines a later cancer. It is, rather, the continued chemical irritation of the products of chronic inflammation which finally induces the malignant change in the epithelial cells. The obvious conclusion from this well-accepted opinion is that cancerous degeneration may be prevented by a prompt restoration of the cervix to anatomic integrity before irritation has had time to exert its baneful influence.

Precancerous conditions of the cervix occur during adult life, but more especially during the third, fourth and fifth decades. They are confined almost entirely to women who have born children. This fact impresses one with the importance and significance of lacerated and infected cervical tissues as precancerous factors. Women who have no cervical lacerations with infections are seldom afflicted with cancer.

And yet this great practical lesson gleaned from the labors of the research-worker, is meeting with tardy response from the clinician. Until recently at least, the practice of primary repair of the lacerated cervix has been almost universally discountenanced. Moreover, one daily sees in the gynecological clinic, patients, with dangerous cervical lesions, who have been advised to defer repair operation until the chance of further child-bearing is past, even if that period be ten or fifteen years distant.

Graves, in order to gain first-hand information on this subject, studied the histories of five hundred thirty eight cases at the Free Hospital for Women and found that only nine or one and six tenths per cent ~~which~~ developed cancer after cervical repair, and, in most of these early pathological records were lacking.

He, approaching the subject from another angle, studied the hospital histories of four thousand eight hundred and fifteen cervical repairs, including the operations of trachelorrhaphy, amputation, and cauteriza-

tion, and was able to find seven cases that later developed cancer. In three cases (including the two mentioned above) the pathologist had overlooked a cancer in the tissue removed by a trachelorrhaphy. In two cases it could be shown that the plastic operation, injudiciously performed, had resulted in extreme obstructing stenoses of the upper vagina and cervix, conditions which we have seen play an important part in the production of genital cancer.

He has, then, out of nearly five thousand cases of cervical repair, the records of only four that developed cancer later, and in two of these the disease was conceivably encouraged by an unskillful operation, or at least might have been prevented by a skillfull one.

It cannot be claimed that his figures constitute an absolutely scientific proof of the prevention of cervical cancer by repair, since it is impossible to gather a series of control cases for comparison. Nevertheless, they are of value in supporting the belief generally held, and now rationalized by science, that timely reparative operations insure an effective, though not a perfect, prophylaxis against cancer.

He summarizes his conclusions by saying that the irritation of a lacerated cervix is a competent stimulating cause of cervical cancer, and that timely repair probably prevents it.

Norris says that cervical cancer is much more insi-

dious and silent than most text books indicate. He believes the sex age not the calendar age to be the predisposing factor.

Graves emphasizes the fact that cancer of the cervix is a peculiarly treacherous disease, in that it does not cause definite symptoms in the early stages and because the first symptom when they do occur are not apt to arouse the suspicion of the patient or of her physician.

He states that leucorrhoea, hemorrhage and pain occur in the order given. Schmitz says, that hemorrhage is the earliest and most alarming symptom, discharge the most repulsive and constant symptom, and pain the most unfavorable symptom.

Davis in a report of one hundred and fifty cases from hospital A gave his conclusions as follows:

(1) The cases of cervicitis and endocervicitis without a single exception gave evidence of some degree of laceration.

(2) The chief complaints were:

Pain in the lower abdomen	48%
Leucorrhoea	32%
Pain in the back	16%
Irregular menstruation	12%
Dragging sensation in the pelvis	12%
Fainting spells	08%

(3) The symptoms were variously associated and a single symptom prevailed as subdominant complaint in a higher per cent of the patients. Eighty-eight per cent complained of leucorrhoea dating always to the last labor, twenty-eight per cent complained of a dragging sensation as a secondary complaint, in twelve per cent being the primary symptom of a retroverted uterus. Those complaining of pain in the back had severe lacerations, long labors and instrumentation with many complications. Headache was a complaint of four per cent. It was more severe in the morning and lasted one to four hours, being occipital or frontal in character.

In the six hundred and thirty-nine cases from hospitals B and C, he found:

(1) Menstrual disorders	58%
(2) Leucorrhoea	49.6%
(3) Pain	
(a) Abdominal	50%
(b) Bearing down pain in lower abdomen	32%
(4) Backache	28%
(a) Dating from last pregnancy	25%

Summary of chief symptoms:

Pain in lower abdomen	49%
Leucorrhoea	41.6%
Menstrual disorders	35%
Pain in back (since last child birth)	22%

The vaginal discharge is due at first to an increase in the normal secretion as a result of hyperemia, and also to a secretion from the newly developed cells. At first, therefore, the vaginal discharge of carcinoma differs from the normal secretion only in quantity and not in quality. Gradually, however, when the walls of the blood vessels, changed by the tumor growth, become more permeable, the secretions become mixed with blood plasma, and hence assume a much more watery character. It becomes offensive sooner or later. It becomes very profuse, especially in the fungating type of the disease and may sometimes entirely replace the bleeding. Occasionally the discharge is purulent from the start, in which event the carcinoma has probably superimposed itself on an area of previous suppuration. Bonney notes two cases in which adenocarcinoma of the cervix of a peculiar type was superimposed on a long continued gonorrhoeal cervicitis, and similar cases are on record. More commonly the discharge becomes purulent coincidental with necrosis and breakdown of the growth.

Ready bleeding of cancer of the cervix from coitus or digital examination is a most important sign, and does not exist to the same degree in any other condition. It generally begins intermittently and may remain so for many months but eventually becomes continuous. It is provoked by coitus, douching or vaginal examination as stated above, and also by effort or straining. Thus, it may only occur during micturation or defecation in which

case it may be wrongly supposed to come from the bladder or bowel. The amount lost varies in different cases being large in some even in the beginning, but more usually not profuse until the disease is well advanced. Finally, there are cases in which the loss is scanty throughout or even no more at any time than a light brownish or pinkish staining.

Pain is usually a later symptom and indicates that the growth has passed beyond the confines of the cervix. There is one exception to this rule, namely, certain cases of very massive infiltrating growths in which pain is evoked by the mere excess of tissue tension in the cervix. The pain is variously felt according to the direction in which the malignant growth is spreading. Thus, ~~it~~ ^{it} may be complained of chiefly in relation to the bladder and the act of passing water, or it may be felt on one or both sides of the lower abdomen and down the inner aspect of the thigh; or it may be located in the sacrum or even in the rectum. Of these various types of pain, that involving the bladder is the most common because it is the nearest neighbor to the cervix and, therefore, the most liable to secondary involvement. As Graves puts it, a cancer situated on the anterior lip of the cervix tends to grow toward the vagina and to invade, by extension, the bladder wall, giving symptoms of cystitis. Pain on micturation does not necessarily mean that the bladder is infiltrated, but it is very suggestive of it, and if in

addition the urine contains pus or blood in it, it is almost certain. In many cases it is a late symptom, but the invasion may occur while the case is still operable. It is a serious complication, however, and in general makes the prognosis as to recurrence particularly bad. The invasion of the ureters by extension into the parametrium may cause symptoms of hydro-ureter and hydro-nephrosis, due to mechanical obstruction of the ureters. Wertheim has shown that the ureteral wall is peculiarly resistant to the invasion of carcinomatous disease, so that the symptoms are due to extensive pressure from the surrounding new growth masses. Pain in the lower abdomen on one or the other side is due to infiltration of the paracervical tissues, and when it is felt down the leg it is almost certain that the cellular tissue lying on the side wall of the pelvis or the glands in that situation, or both, are affected. Pain in the back indicates that the posterior parts of the uterosacral ligaments are being infiltrated, whilst pain referred to the rectum itself, usually connotes that the growth is actually invading the bowel wall.

It sometimes happens that infiltration from the cancerous growth extends to the parametrium and pelvic peritoneum. This is especially true of the infiltrating endocervical cancer that forms in the posterior lip and eats its way into the stroma of the cervix toward the posterior cul-de-sac. Such infiltrations produce the symptoms characteristic of a pelvic inflammation.

In very advanced stages the external genitalia may become greatly swollen on account of thrombosis of the pelvic veins. General metastases to distant parts of the body are surprisingly rare, and often do not occur even in the last stages.

Discharge, bleeding and pain in that order of appearance are almost universally recognized by the profession as the classical symptom picture of carcinoma of the cervix uteri, but an inverted sequence is not uncommon. The pain is variously misinterpreted as due to sciatica, colitis, enteroptosis or neurosis. This causes an overlooking of the true cause until too late. The result is that by the time a show of blood or other unusual discharge draws attention to the genital region and compels an examination, the growth is usually too far advanced for any treatment to be likely of success.

The general constitutional symptoms of advanced carcinoma of the cervix are especially marked by anemia, continual fever and by extreme cachexia.

The anemia is one of the most prominent symptoms and may be due to hemorrhage, to absorption of hemolytic agents from ulcerating or infected surfaces, to toxic substances elaborated by the tumor itself, or to the distribution of nutrition. Benign tumors have little or no effect on the blood and the early effect of malignant tumors is slight. There is also a lowered color index.

All cases of hemorrhage from any source or grave anemias should be thoroughly investigated to eliminate

the possibility of cancer. One must rule out tuberculosis, ulcers of the intestinal tract, varices of the esophagus, cirrhosis of the liver, syphilis, nephritis, parasites, splenic and blood disorders, menorrhagia and hemorrhoids.

The elevation of temperature is variously explained. It is probable that the difference in the type of fever which various cases show, bespeak differences in the cause. High, continual and remittant fevers are characteristic of sepsis and pyemia, and are to be referred to the activity of the bacteria which infect the cancerous mass. Sapremic fever with a lower pulse rate than that of the septic type is due to the absorption of the decomposing cancer tissue. Irregular elevations of temperature are caused by the destruction and absorption of the protein material, as in necrotic fibroids and disintegrating hematomas. Patients with advanced carcinoma of the cervix show marked improvement after radiation or the palliative operation of curettage and cauterization of the excrecent masses, the improvement being largely due to a diminution in the amount of toxic absorption. Temperature elevation does not ordinarily appear in the primary stages, so that it is of no great value in making an early diagnosis.

The cachexia that results from cancer of the cervix is extreme, being rarely equalled in any other form of cancer in the body, and it is a fit setting for this gruesome disease. It is accompanied with great emaciation,

but neither cachexia nor loss of weight is apparent during the early stages. The causes which contribute to this cachexia are lessened nutrition from loss of appetite and hemolytic changes in the blood, due to absorption of toxic products from bacterial processes or from protein destruction.

Malinin describes the causes of the cachexia in advanced carcinoma of the cervix as follows:

(1) The toxins produced by the malignant growths act on the Malpighian Corpuscles of the spleen, causing hypertrophy of the phagocytic elements and increased destruction of erythrocytes.

(2) The destruction of the red cells in the spleen and lymphatic glands plays an important part in causing the anemia found in cancer cachexia.

(3) Death in this cachectic state is to a large extent the result of the perverted functions of the blood forming organs.

One must eliminate cancer as the cause of loss of weight, but it should be borne in mind that other conditions may be the cause of it, such as tuberculosis, diabetes, toxic goiter, benign stricture of the esophagus, dieting, low protein or food intake and vomiting from any cause, as in pregnancy toxemias, pyloric obstruction and gall bladder disease.

Novak believes that physicians should throw away their mental conception of cancer if it is a picture of a large cauliflower growth on the cervix or a large foul,

ulcerated, excavated cancer ulcer. For what good accrues? None. It is then too late for anything to be done. It is far better to be able to recognize the disease early in its course.

Schmitz believes that the surgical and radio methods of treatment of carcinoma of the cervix uteri have been technically so perfected that further improvement cannot be expected. He says that improvement can come only from earlier diagnosis and subsequent immediate treatment.

The careful consideration of an unsuspected malignancy in making a diagnosis is becoming more necessary for the following reasons:

- (1) The increasing prevalence of malignancies.
- (2) The necessity for the early discovery of cancer if any hope is to be entertained for the cure of the patient.
- (3) Most cases of malignancy are implanted upon other chronic diseases.
- (4) Secondary malignancies are often confused with other diseases, and the primary growth may or may not have been discovered.
- (5) Unnecessary operations and treatments can be avoided if the presence and existence of metastases are recognized.

The main facts that militate against early discovery of primary cancer are:

(1) Cervical carcinoma is insidious in its onset and does not exhibit early alarming symptoms. Pain, loss of weight, anemia and hemorrhage are generally advanced symptoms.

(2) Cancer in women occurs with the greatest frequency in the uterus and cervix. These organs are the seat of so many chronic disorders that the symptoms due to a beginning malignancy often are undiscovered or unrecognized. Oftentimes the physician whom she consults advises waiting, especially if she is under the so called "cancer age". Women who have borne children and have a torn cervix with its accompanying leucorrhoea do not consult a physician when there is a change in the character of the discharge. They are often sensitive about being examined and wait until they are beyond help. Too often the physician treats the matter of an ulcer or erosion of the cervix too lightly, and does not make careful and repeated examinations for a possible malignancy.

(3) The more or less acute onset in a few cases also confuses the diagnosis.

(4) Physicians often do not recognize the fact that carcinoma is found more often in younger people than formerly and fail to consider the possibility of cancer in persons under the so-called "cancer age". Joseph Colt Bloodgood states: "Carcinoma as a cause of death is on the increase and has gradually risen from the twentieth place nine years ago to the second place in nineteen twenty-nine."

Before proceeding on with a general discussion of the diagnosis of carcinoma of the cervix uteri, there are several general rules which should be recalled and kept in mind.

(1) Cancer does not grow in healthy tissues or organs.

(2) Cancer begins in a spot or focus, the cells of which at first are not malignant or atypic, but of an inflammatory nature.

(3) Chronic mild irritations and low degree infections cause or work on these foci and produce the changes characteristic for malignancy.

(4) All tumors grow to some extent before causing symptoms.

(5) The discovery of cancer during this symptomless silent period and the immediate application of adequate treatment would put us in the control of the disease.

(6) If physicians became cancer minded, i.e., would keep in mind the possibility of malignant disease in chronic tissue changes, then diagnoses would be rendered without delay.

(7) The avoidable delay by the physician, i.e., placing the patient under observation instead of making an immediate diagnosis and applying treatment forthwith if cancer is found, is responsible for the poor end results of treatment

(8) It seems highly probable that the first stage of cancer of the cervix proceeds from a chronic cervici-

tis which presents either papillary erosions or follicular nodes and results from an inflammatory exudate which is not sufficiently fulminant to destroy the epithelial layer but to cause the cells to proliferate forming papillary erosions or Nabothian cysts. Hence prophylaxis means treatment of chronic cervicitis.

In most instances, when the diagnosis is concerned with early stages of the malignancy, the cervix should be examined in two imaginary plains. The more nearly normal half should be recognized first and should receive first attention. The second half can next be subjected to both comparative and exclusive examinations.

The posterior lip will be found more frequently the site of pathology. The margin of the portio is the site of most cancer, and the growth in its earlier stages is in most instances shallow, partly eroded or ulcerated, and slightly sorter than normal epithelium. The adjoining tissue is denser than normal and the area involved has the appearance of being chronically inflamed at or very near the site of an old laceration. The suspected tissue, if stained, will absorb enough more pigment to make a contrast with the uninvolved tissue about it.

History of previous child birth, miscarriage, instrument trauma, gonorrhoea or other inflammations with leucorrhoea, will always add to the sum total of obtainable data favoring malignancy.

The life of a patient suffering with cancer of the cervix depends on early detection of the disease. Since

the cancer is always accessible, mistakes in diagnosis should not occur if proper measures are observed. The requisites for making a diagnosis are familiar -- with the early symptoms and pathology of the disease, some experience in making vaginal examinations and a quick resort to biopsy if there is the faintest doubt.

The full blown carcinoma of the cervix is obvious to the veriest ^{est} tyro. The fungating easily bleeding foul smelling mass of the everted type is simulated only by a necrotic pedunculated fibroid. Still more characteristic is the sloughing excavation of the ulcerative type with its hard irregular edges and general infiltration and fixation of the surrounding tissues. In these advanced forms the pale watery discharge of pinkish or dirty hue, the unmistakable fetid odor, the anemic and wasted appearance of the genitals and the immediate profuse bleeding on touching the tumor are all signs each one of which is almost pathognomonic of the disease.

The development of a cervical carcinoma according to macroscopical examination may be considered under three stages : the nodular, the ulcerative, and the necrotic stages. They may be observed in the three locations in which cancer usually originates -- namely, the vaginal portion of the cervix, the cervical mucosa, and the endometrium.

The diagnosis of the first or nodular stage of carcinoma of the vaginal portion of the cervix cannot be made by inspection or palpation because nodules of

benign nature are seen more frequently than nodules of a malignant character. Harmless nodules are the follicular erosions. If they are punctured, mucus exudes. Should the puncture cause bleeding then a diagnostic excision must be made, for the nodule is probably malignant. The subsequent histological examinations alone can give us a positive diagnosis.

The second stage of carcinoma is that of ulceration. It results from the characteristic and peculiar tendency of carcinoma cells to degeneration or decay. This tendency is possessed by all malignant growths and is caused by poor blood supply. The ulcers are usually deep, are excavated, have sharp mouse-eaten like edges and an indurated periphery. The ulcerations must be differentiated from papillary erosions. If an ulcer of the vaginal surface of the cervix is touched with a cotton applicator and does not bleed it is probably benign. The carcinoma ulcer, however, bleeds on local irritation and the blood is arterial and the flow is continuous. A diagnostic excision should be immediately made and the excised tissues examined microscopically to determine its benign or malignant nature.

These two initial stages do not cause specific symptoms unless irritated locally as by a gynecological examination or cohabitation. A more or less profuse discharge without color or odor may be present, probably resulting from the co-existing inflammation.

The third stage of portio carcinoma shows friability or necrosis of tumor tissues. The tendency to central necrosis or friability is a characteristic sign of advanced cancer disease. It is always accompanied by a reddish brown or sanguinous discharge, and as infection rapidly ensues, a cadaveric or putrid odor becomes associated. Hemorrhages at irregular intervals usually occur after local irritation.

The differential diagnosis of portio cancers comprises not only the follicular and papillary erosions but also tuberculous ulcers, luetic chancre, chancroid and sarcoma. The microscope and blood tests will aid in the determination of the nature of the lesion.

The first sign of carcinoma of the cervical canal mucosa and the body of the uterus is irregular hemorrhages. These cancers are especially deceiving because the external os and the vaginal mucosa may appear perfectly normal. If under strictest aseptic precautions a sound is introduced into the cervical canal or the uterine cavity and a thin stream of bright red blood escapes from the cervical canal, then this observation may be regarded as highly suspicious of malignancy especially if the trickling of blood continues for some time after the manipulation. These signs are a contributory means of arriving at a diagnosis and should not be conclusive. Hence, dilatation of the cervical canal, diagnostic curettage and immediate frozen tissue examination must be done to render an immediate and correct diagnosis.

In the early inverting form the cervical lip is hard, nodular, and irregular, usually bleeding a little on examination. The portio may be entirely intact and on inspection excite little or no suspicion. In elderly women the atrophied cervix may have disappeared and in its place can be felt a stiff, nodular puckering of the upper vault of the vagina. For the diagnosis of inverting cancer the sense of touch is much more accurate than inspection. In most cases a small curette passed through the external os will bring forth a small crumbling bit of tissue with profuse characteristic bleeding. If the curette fails to find friable tissue and the bleeding is slight the case is probably one of atrophy or chronic cervicitis.

But to get back to the diagnosis of early carcinoma. Dr. Schiller attempts to make early diagnosis of carcinoma by use of the microscope and sections of cervical tissue. There is, he claims, a type of tissue change which is to truly developed carcinoma as an embryo is to the adult. He believes he has found this carcinomatous layer, as he calls it, around a definite cancer growth and separating the true cancer from healthy tissue. This carcinomatous superficial layer differs from the character of an advanced carcinoma because it neither ulcerates superficially nor does it invade deeper tissues. However, from the histological point of view, this layer shows the characteristics of carcinoma -- atypical and polymor-

phous cells and frequently plenty of mitotic figures. In addition there is no histological difference whatsoever in the area where the carcinomatous zone passes into the deeply penetrating carcinoma, while there is a distinct histological difference at the point where the carcinomatous layer is marked off from the epithelium.

Schiller states his hypothesis thusly -- "If the carcinomatous area bordering the carcinoma is recognized as carcinoma, and we are logically bound to accept this assumption as true, then from our study of the uninterrupted series the smallest carcinomatous layers with no down-growth must be considered carcinoma as well." He then proceeds to describe in detail this carcinomatous layer from a histo-pathological standpoint. He claims to have found a great majority of specimens in leukoplakic areas.

To locate the suspicious areas, Schiller made vital stains with Lugol's solution. In the normal cervical epithelium there is glycogen -- there is none in carcinomatous epithelium. This glycogen is stained by Lugol's iodine solution. The normal epithelium requires about one half to one minute to attain a mahogany-brown color. "However, in the areas in which some pathologic process is present no brown staining takes place and the epithelium remains white and unstained."

"The technique used in painting the cervix is as follows: A cervical speculum is placed in the vagina and out of a small cup with a long spout, about ten to

fifteen cubic-centimeters of Lugol's solution is poured and spread with a tampon over the cervix and left in the vagina for about a minute. The iodine solution is then sucked off with a tampon, the cervix and vagina are cleaned of the excess liquid, and gently wiped. It is necessary that the solution should moisten the entire cervix and that no fold should prevent the entrance of the liquid as that might cause a wrong diagnosis. If the epithelium shows an unstained spot we must be suspicious of carcinoma and the tissue here must be examined histologically. As a rule the presence of white, unstained epithelial spots which are free from glycogen may indicate four possibilities.

(1) The presence of carcinomatous layers or of incipient carcinoma.

(2) The presence of hyperkeratosis, as a result of prolapse or descensus vaginae.

(3) The presence of hyperkeratosis, a consequent of lues.

(4) Glycogen bearing upper layers having been removed by force.

The group is determined by microscopic examination only, with only a small piece of unstained tissue taken from the white layers but never from within dark-red, eroded or ulcerated parts.

This technique has been used to determine the extent of the carcinoma. All carcinoma are surrounded by this carcinomatous layer which if left makes recurrence

inevitable. The method is inexpensive, easy, simple and short. "It makes possible the diagnosis of a carcinoma of the cervix in its very first stage -- a factor of much importance in securing absolute healing." This method is only good for carcinoma on the cervical surface. However other kinds are relatively rare.

For inner cervical cancer scrape the canal and stain the tissue with Bell's carmine. The presence of large, typical, vesicular, superficial layer of cells with an abundance of glycogen is positive evidence against carcinoma. In his clinic, by this method of diagnosis, Schiller has raised the per cent of complete cures to ninety to ninety-five per cent. Errors of diagnosis have decreased to one and forty-one one hundredths per cent.

Graves, in his article, condenses the work of Schiller into more definite concise terms pregnant with future possibilities for the test. He carefully mentions, however, the limitations of the test and also conditions which obscure it and with which the examiner should be thoroughly familiar. "The test, simple as it seems, is not without its limitations. It appears to be completely reliable when it is clinically negative, that is to say, when all the tissues take the normal stain." The test, therefore, when Negative is specific. However, there are several conditions influencing a positive reaction which must be constantly kept in mind. These are as enumerated:

- (1) The stain does not take on glandular epithe-

lium, like that of the endo-cervix. Hence an eversion would appear pink. The same is true of the epithelium of an adeno-carcinoma, so that this type of cervical cancer must be sought for in the usual manner. Fortunately it is rare.

(2) Ulcerations and erosions do not take the stain since they have no epithelial covering.

(3) In areas of chronic cervicitis, the epithelium seems often to be deficient in glycogen, taking a very light brown which blends with the surrounding deeply staining tissue instead of being sharply defined from it, as in cases of true cancer.

(4) The normal stain is prevented or obscured by slight trauma, such as that from tenacula or scrubbing with gauze. This is caused by the rubbing off of the upper layers of epithelium in which the glycogen is chiefly deposited.

(5) The cervix and vagina of the hypoplastic and atrophic individual stains lighter than the normal. It is especially deep during pregnancy.

(6) Pus stains black since leucocytes are rich in glycogen. Necrotic tissue also stains black, but clear, living granulations do not take the stain. Blood and douche water obscure the reaction.

(7) Hyperkeratous prevents the stain, as in leucoplakia, lues, and exposed areas in prolapse.

(8) The test is of limited value in diagnosing advanced carcinoma, since the superficial assimilatory

stage is usually lost in the melee of self-reproducing cells. Sometimes superficial areas detectable by the Lugol test may be found beyond the border of the advanced cancer, especially in the fornices of the vagina and this may serve as a guide in determining the limits for a radical operation. Cancer cells in the advanced stage may regain glycogen and thus give a dark stain with the Lugol's solution. Normal epithelium lying above an invading cancer takes a normal stain as would be suspected.

(9) Schiller's test is specific for cervical cancer, and is not adapted to other superficial cancers such as those of the vulva and skin in other parts of the body. This is due to the fact that the normal epidermis of the portio and vagina is not cornified and that the upper layers of cells contain a special chemical type of glycogen.

Graves' comment on this intriguing subject echoes opinions of men all over the world, and is as follows -- "We are finding the Schiller test an indispensable aid in the search for early curable cancer of the cervix. It is a specific for the absence of cancer. Failure of the stain indicates certain other abnormal conditions, two of which, leucoplakia and intensive cervicitis are potential precursors of carcinoma and require treatment. We recommend the test for trial to the general profession."

Since we have mentioned so frequently the necessity and value of a routine biopsy on all suspicious cases, perhaps it would be well to give some space in this thesis

to the method and means of taking biopsies.

In the selection of biopsy material, diagnostic responsibility is divided between the clinician and the pathologist. The tissue section may be taken haphazardly or often due consideration for the ocular appearance and palpatory information. The ocular examination may be systematized by noting: (a) malformative, (b) vascular, (c) inflammatory, (d) degenerative, and (e) neoplastic changes.

The malformations will include hypertrophies, hyperplasias, atrophy, scars, ulcerations and neoplasias. The first three are observed accompanying vacular hyperactivity, while the second group have vascular hypoactivity.

The frequency of infections in association with hypertrophy, hyperplasia, ulceration and neoplasms is well known and should always be kept in mind when inspecting the cervix.

An effective ocular examination will obtain information as to size, color, formation, position, discharge, loss of tissue, irritation, presence of cysts, scars, and benign and malignant new growths.

The biopsy section should be about 1.5 x 5 centimeters, and is obtained by cutting from the shoulder of the portio upwards through and past the internal os for about 0.5 centimeters. In Davis' series of twelve hundred biopsies, two-hundred and fifty-three sections were taken without inclusions of squamous epithelium, and

three hundred were without gland tissue. The histopathologic diagnoses consequently reached an efficiency of only seventy-five per cent, solely because of incomplete biopsy sections. This would constitute a serious omission for clinicians who rely implicitly upon the biopsy diagnosis.

May a case report taken from Dr. Lupten's article be introduced? This illustrates very well the sequence of symptoms in carcinoma, the lack of attention paid to the first symptoms, although the patient did her part, the effect of radium on the symptom, and the hopelessness of cure after pain as a symptom has made its appearance as well as the unusual occurrence in a woman of her age.

O. B., colored, age twenty, married, multipara, was first seen October thirteenth, nineteen twenty-seven. She gave the following history: About eight months previously she noticed a whitish vaginal discharge. There was a gradual increase of the discharge and it became slightly yellow. She first sought aid at a local clinic, about three months after first noticing the leucorrhoea. She was given a powder for a douche, but a month later or four months after appearance of the leucorrhoea she began to flow more frequently than usual.

At first there was only a slight increase of irregularity, but the condition soon became worse until she was flowing two or three times each month. At that time she decided to call a private physician, which was about three months after the beginning of irregular and exces-

sive flowing. He made a bimanual examination, but the examination was at home and he did not use a speculum, the diagnosis not being determined. The bleeding continued to get worse and when she came to see Dr. Lupton, she stated she had flowed every day for the past twenty days. This was eight months since the leucorrhoea began.

The following condition was found on examination: the cervix had a cauliflower appearance and it was about the size of a large English walnut. There was considerable raw surface and the bleeding was profuse. The mass was bleeding so freely that it was necessary to keep sponging almost constantly to get a good view. The mass was necrotic and two pieces of tissue, each of which was about an inch long, one half inch and one eighth inch thick came from it during sponging. The cervical canal could not be seen, but was felt anterior, the mass originating from the posterior lip. The fundus was slightly posterior, but was of normal size.

There was no particular tenderness of the adnexa and there was no fixation of the uterus. The patient stated she had very little pain. The sloughed tissue was examined by Dr. E. L. Straul, pathologist at the Norfolk Protestant Hospital, who stated the tissue block was not adequate for the demonstration of all the pathology common to malignancy, but as far as it went it justified the probable diagnosis of malignancy. From the histology, the appearance of the mass and from the pathologist's re-

port it was felt certain that the condition was one of malignancy.

Under anesthesia a biopsy was done on the mass and four radium tubes implanted for forty-eight hours. The bleeding continued to show a gradual decrease, and there was a gradual decrease of the purulent discharge after the first week.

By December tenth or about seven weeks after the application of radium, the bleeding from the cervix had entirely ceased, and by January fifth, nineteen twenty-eight there appeared to be practically complete epithelization of the cervix. During this period the cervix had gradually decreased in size, until it was only twenty-five per cent larger than a normal cervix. At this time the patient was feeling considerably better; she had gained some weight; there were no masses in the adnexa or any evidence suggestive of metastases so we thought she had an excellent chance for a cure. During the latter part of February, however, she began to have a purulent discharge and a few days later she began to bleed. On inspection of the cervix it was found that the bleeding was coming from the posterior lip and from the cervical canal. At that time a small firm mass about the size of a small bird's egg had developed in the right adnexa.

On March ninth, nineteen twenty-eight, fifty milligrams of radium were inserted into the cervical canal, remaining in place for twenty-four hours. The patient felt

fairly comfortable until March thirteenth, when she developed considerable pain in the right lower abdomen. There was considerable tenderness and rigidity in the right lower quadrant. The bleeding had ceased, but there was a profuse purulent discharge. Fever developed, the pain and tenderness increased and the upper part of the right thigh began to swell. It was first thought that these symptoms might be the result of a thrombophlebitis. Although the patient's general condition appeared improved for a while, the mass in the right adnexa increased in size. There was practically very little pain in the right thigh. It then became more evident that the swelling of the thigh was due to involvement of the pelvic lymph glands, though part of the condition resulted from the infection.

On June third, nineteen twenty-eight, the patient was sent back to the hospital, and it is to be noted, she had been unable to be out of bed since the last application of radium. The temperature was 102° F. and the pulse was 104. The blood examination then was as follows: Red blood cells 3,330,000, white blood cells 220,400, polys 79%, Hb. 60%. Laparotomy was advised because it seemed evident there must be some pus present, but the patient refused operation. She continued to run a septic temperature and the pelvic mass grew more pronounced. She later consented to an operation and on June eleventh a laparotomy was performed under ethylene anesthesia. There was an inflammatory mass involving the uterus, tubes, ovaries, and a small part of the small intestine, which filled the

right half of the pelvis and extended above the pelvic brim . Even though there was considerable pus present and most of the mass was evidently inflammatory, it was felt certain that part of the mass was due to metastasizes.

The swelling in the right lower abdomen and in the right groin increased until there was some fluctuation, and it was evident that there was some free pus in the abdomen. On August sixteenth, nineteen twenty-eight, forty-five cubic centimeters of a purulent and partly gelatinous substance was withdrawn from the area of fluctuation in the right lower abdomen. We continued to withdraw about two hundred to three hundred cubic centimeters of fluid from this area twice weekly. It should be stated that long before this fluid accumulated the advisability of another laparotomy was discussed and it was thought inadvisable.

About the last of August an incision was made in the right lower abdominal wall just above the outer half of Poupart's ligament and the wound drained. Both the abdominal wound and the incision in the abdominal wall continued to drain freely. The patient's condition was rapidly getting worse and she insisted on going home August thirty-first, nineteen twenty-eight. Her condition continued to grow worse and she died September twenty-eighth, nineteen twenty-eight, which was less than one year from the time she was first seen. We were unable to get an autopsy, and even though this patient had

a severe septic condition, we are confident there was marked metastasizes from the cervix. It is probably safe to assume that metastases had already occurred when this patient was first seen, even though no evidence of metastases could be made out. Our principle regret in this case, however, is the fact that the patient was not seen earlier.

It is now rather generally accepted that cancer is a process characterized by an unrestrained growth of cells of the body. This growth seems to start at one or more focal points and in many instances to be preceded by a phase of relatively long duration, during which the cells are acted upon by something associated with a process of chronic irritation, which results in cellular hyperplasia. In its incipency cancer is generally localized but sooner or later it spreads by invading surrounding tissues and cancer cells are often carried to distant regions by way of the lymphatics, the blood stream or the body cavities where they become reimplanted and continue to grow. In their growth, they reproduce the tissues from which they come but always in a more or less atypical fashion. In general the relative malignancy of a neoplasm is indicated by the degree to which the tissues it forms vary from normal tissues, but the application of this principle has not yet reached a high degree of accuracy and reliability. The unchecked growth of cancer results in the death of the

host, as a rule, in a few months to a few years from the first appearance of symptoms dependent in part upon the site of origin. Sometimes the cancer progresses very slowly so that the individual may survive for twenty-five to thirty years, but this is uncommon except in the case of certain skin cancers.

The early stages of cancer growth, especially of the cervix uteri, are associated with symptoms that can be determined. Yet even when it begins to occasion symptoms they are often so vague as to leave the carcinoma unrecognized unless the diagnostician is "cancer conscious" and makes a special effort to look for it.

It is in this silent and insidious onset that the tragedy of cancer lies, for it delays the treatment in many instances until after the growth has ceased to be localized, at which time the chances of eradication are enormously decreased. At the present time there are only two methods of dealing with this disease after it has made its appearance: mechanical removal and destruction of the neoplastic cells by some form of selective irradiation with radium or Roentgen ray. That cancer therapy today has not succeeded in checking the steady year by year increase in the cancer mortality rate is common knowledge.

In the majority of the countries where statistics are reliable, cancer of the uterus is one of the most frequent causes of cancer mortality in females. There is

some variation about this which has not been explained. In England it is exceeded only by the breast and in the United States it is the most frequent cause of death, but in Norway and Holland it is greatly exceeded by the gastro-intestinal tract. In Japan it is slightly exceeded by the stomach liver group, although not to the same extent as in Holland. The death-rate in these various countries is almost stationary for cancer of the uterus, and all the tremendous efforts which have been concluded on prophylaxis, early recognition and treatment have had no apparent effect upon it.

The portion most frequently affected is the cervix and here its development often follows the very common lesions of chronic endocervicitis, the chief cause of which is found in neglected injuries received during child-birth. Although this has been recognized for some years, and the importance of repair of cervical damage after delivery and subsequent treatment of cervical erosions and inflammations has been repeatedly urged by obstetricians and gynecologists, the actual proportion of women who receive proper treatment for these conditions is negligible; certainly not enough to affect the incidence of cancer. Moreover, the warning to the public not to neglect discharge and hemorrhages, particularly after the menopause, and to physicians never to fail to inspect, palpate, curette and biopsy all such cases, seemingly has had no general effect that can be appreciated. Gornick (1929) remarks sadly that the proportion of in-

operable cases coming to the Frankfort Gynecological Clinic (45%) is exactly the same as it was in nineteen nineteen, and that this seems to be the case everywhere. Regaud (1929) and his associates at the Curie Institute found that if the disease is treated in its earliest stages by experts, three quarters of the patients can be cured clinically and can have a reasonable expectation of remaining alive and apparently cancer-free for five years, and probably much longer. But such results are attained in relatively few cases and represent the ideal. Many come for treatment to a few institutions where adequate treatment is given only when one quarter of them can be saved, and the large majority who are not cared for by experts do not even have this slender chance afforded them and succumb to the unchecked ravages of their disease. This, although it has been demonstrated that the death-rate from uterine carcinoma could be reduced if adequate treatment could be afforded to all women suffering from it, the actual fact is so few receive it that the mortality-rate has remained unaffected.

Epithelioma of the cervix and to a less extent carcinoma of the body of the uterus are the two chief malignant tumors of the uterus. There are other malignant tumors, notably the interesting chorionepitheliomas, sarcomas, and malignant teratomas, but as a rule they are so unusual as to have slight economic importance in comparison with the two commoner varieties.

Such are some of the reflections to which a consideration of this great theme -- cancer -- arouses in the student. No problem in surgery has been longer debated; none is of wider interest; none has bred keener disputants and none furnishes a more absorbing, or a more promising subject for the investigator trained in the modern methods of research.

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